

### **REMARKS**

Applicants' representatives thank the Examiner for the courtesy of a telephone interview conducted on February 27, 2006. The present response addresses substantive points discussed during the interview. Specifically, amendments to claim 188 were discussed, as well as the teachings of Graham, *et al.*, Int. Pat. Apl. Pub. No. WO 97/05280. It is believed that many or all points were successfully clarified in the interview, and Applicants' position on these points is memorialized herein in the present response. Accordingly, the present response is believed to constitute a complete written statement of the reasons presented in the interview as warranting favorable action, as required by 37 C.F.R. §1.133.

Independent claim 188 has been amended to recite a method for determining the sequence of at least a portion of a DNA or an RNA strand, comprising fragmenting one or more bases from a DNA or an RNA strand using a nuclease to form a plurality of fragments, each fragment comprising at least one base; sequentially identifying each of the one or more fragments by Raman spectroscopy; and determining the sequence of at least a portion of the DNA or RNA strand based on the sequential identification of each of the one or more fragments. Support for this amendment can be found in the specification, for example, on page 15, lines 17-33. Accordingly, no new matter has been added.

In addition, claims 189, 195, and 198 have been amended to provide proper antecedent basis with respect to the above-described amendments of independent claim 188. In addition, new dependent claims 199-201 have been added. Support for these amendments can be found in the specification, for instance, on page 15, lines 17-33. Accordingly, no new matter has been added.

The specification has also been amended to recite thymine, adenine, cytosine, guanine, or uracil as examples of nucleotides. Support for this amendment can be found in claim 19 as originally filed (page 25, lines 27-28). Accordingly, no new matter has been added.

After these amendments, claims 188-195 and 198-201 are pending for examination, while claims 1-17, 19, 23-37, 39, 43-58, 60, 64-72, 74, 78-85, 87, 91-117, 122, 125, 126, 128, 130, 132-135, 138, 139, 146, 147, 153, 155-157, 159-162, 164, 172, 179, 180, 182, 183, 187, 196, and 197 remain withdrawn.

Rejections under 35 U.S.C. §112, ¶1

Claims 188-195 and 198 have been rejected under 35 U.S.C. §112, ¶1, as failing to comply with the written description requirement.

Applicants do not concede to the accuracy of any of the rejections under 35 U.S.C. §112, ¶1. However, in light of the above-described amendments made with respect to independent claim 188, and as discussed with the Examiner in the February 27 interview, it is believed that claim 188, as amended, finds written description support in the specification. Accordingly, it is believed that this rejection is now moot, and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, ¶2

Claims 188-195 and 198 have been rejected under 35 U.S.C. §112, ¶2, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as to the invention.

Claim 188 has been rejected as lacking "a stated goal which should be recited in the preamble," for having insufficient antecedent basis for the term "the sequence," and for not clarifying how multiple nucleotides can be removed from a single nucleic acid. It is believed that the above-described amendments to claim 188 have addressed these issues, and it is therefore respectfully requested that this rejection be withdrawn. However, Applicants note that they are not aware of a requirement under §112, ¶2 that a preamble is required to recite a stated goal, and thus do not concede to the accuracy of this requirement.

Regarding the rejection of claims 190-195, from the February 27 interview Applicants believe this was based on the Examiner's impression that it was unclear where the specification discloses labeled nucleotides, such as thymine, adenine, cytosine, guanine, or uracil. Applicants note that the specification explicitly discloses thymine, adenine, cytosine, guanine, or uracil in claim 19 as originally filed (page 25, lines 27-28), and in the specification now amended. Further, the specification discloses that fragments of DNA or RNA can be labeled (page 8, lines 9-11).

Rejections under 35 U.S.C. §102(b)

Claims 188-195 and 198 have been rejected under 35 U.S.C. §102(b) as being anticipated by Graham, *et al.*, Int. Pat. Apl. Pub. No. WO 97/05280 ("Graham").

As discussed in the February 27 interview, Applicants do not see where in Graham is there a disclosure or a suggestion of fragmenting one or more bases from a DNA or RNA strand using a nuclease, and identifying each of the fragments by Raman spectroscopy. Although Graham discloses sequencing nucleotides in example 9, pages 80-84, the sequencing in Graham is performed by hybridizing nucleotides to a template in the presence of a polymerase, dNTPs (nucleotides), and chain-terminating nucleotides (ddNTPs), which stop further elongation of the nucleotide sequence when incorporated into the growing nucleotide strand. By identifying the lengths of each of the various strands grown in this procedure (each of which ends in a predetermined chain termination nucleotide), the sequence of the template can then be determined. However, Graham does not disclose a step of fragmenting the nucleotide strand, and in fact teaches away from such an act, as fragmenting the nucleotide strand would confuse subsequent analysis.

Furthermore, on pages 53-57, the sequencing technique of Graham is described in additional detail, in which chain-terminating nucleotides (dideoxynucleotidetriphosphate bases, or ddNTPs) are used in a "Sanger" type chain termination reaction. The nucleotides grown during the Sanger-type chain termination reaction may then be sequenced, as described above. Although a SER(R)S label is mentioned, it is not used for sequencing the nucleotide strand, but is complexed to the nucleic acid as a label to identify a particular nucleotide strand to be sequenced (p. 52), i.e., the SER(R)S label is merely used to detect the presence of a target nucleic acid in a sample (abstract).

Accordingly, Graham does not teach or suggest independent claim 188, and it is therefore respectfully requested that the rejection of independent claim 188 be withdrawn. The remaining claims each depend, either directly or indirectly, from independent claim 188, and are believed to be allowable for the above-mentioned reasons. Withdrawal of the rejection of these claims is also respectfully requested.

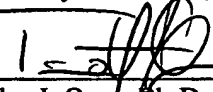
**CONCLUSION**

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the undersigned at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

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Respectfully submitted,

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